

Application No.: 10/072,320

Response to Office Action  
Mailed December 23, 2008**REMARKS/ARGUMENTS****A. Status of the Claims**

Claims 33-57 were pending, with claims 48-50 and 52-55 having been withdrawn, at the time the Action was mailed. Claims 33, 35, 38 and 40 have been amended, as shown above and discussed in greater detail below. No new matter was added in any of these amendments. Claim 45 has been corrected to remove a comma, bringing this claim in line with the originally filed claim. As such, claim 45 has not been "amended," and certainly no new matter was added by this correction. No claims were cancelled or added. Therefore, claims 33-57 are currently pending, of which claims 48-50 and 52-55 are withdrawn.

**B. Amendments to the Specification and the Claims**

Claim 33 has been amended to incorporate several, but not all, of the limitations of claim 35. Claim 35 was amended accordingly. Support for both amendments is provided by claim 35 as originally filed and by the diagram shown in the lower portion of Figure 1.

The Specification and claims 38 and 40 were amended to correct the weight percentages of the water-insoluble swellable mucoadhesive polymer and the pH-sensitive film-forming polymer. The previous ranges corresponded to the gel aspect of the invention, but not to the bi-layer wax-film composite aspect, which corresponds to the aspect to which the claims of this divisional application are directed. Support for the ranges as amended is provided in Table 1 (page 30) and Figure 2. The ratios of Noveon to Eudragit are given as 33-80% w/w Noveon and 20-67% w/w Eudragit which corresponds to 1:2 to 4:1 in Table 1. None of these amendments result in the addition of new matter.

**C. The Indefiniteness Rejection is Overcome**

The Action rejected claim 45 for indefiniteness because of the term polyvinyl. The Action treated polyvinyl as it appeared in the previous Listing of Claims, namely as a term

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separated from its neighboring terms by commas. In fact, it appears that an extra comma was accidentally inserted between the terms "polyvinyl" and "pyrrolidone" during the prosecution of this application. As originally filed, claim 45 had no comma between these two terms. Instead "polyvinyl" immediately preceded the term pyrrolidone. Claim 45 as originally filed is shown here:

45. The water-soluble or swellable polymer of claim 42 where said water-soluble or water-swellable polymer is tragacanth, polyvinyl pyrrolidone, polyvinyl alcohol, cross-linked polyacrylic acid, polyethylene glycol, a cellulose polymer derivative, or other suitable pharmaceutical polymer that is water-soluble or water-swellable.

Furthermore, claim 45 was never amended during prosecution. Instead claim 45 was carried forward as an original claim since the filing date of this application—February 7, 2002. The above Listing of Claims removes the extra comma and thus restores this claim to its originally filed state. For at least these reasons and because the term polyvinyl pyrrolidone is well known to a person skilled in the art, the indefiniteness is moot. Applicants therefore respectfully request that this rejection be withdrawn.

**D. The Obviousness Rejections are Overcome**

**1. Obvious Rejection over Suzuki**

The Action rejects claims 33-34, 42-45 and 56-57 as obvious over U.S. Patent 4,715,369 to Suzuki *et al.* ("Suzuki"). Applicants respectfully request the Examiner to reconsider and withdraw this rejection in view of the comments below.

First Suzuki fails to teach all the limitations of the claimed invention. Applicants were aware of Suzuki at the time of filing this Application and summarized its teaching in the background section of the Application, reprinted here:

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U.S. Patent 4,715,369 by Suzuki *et al.* relates to methods to treat the injured oral mucosa with a thin two-layer tablet comprised of both an adhesive layer and a nonadhesive layer. The adhesive layer is comprised of water-soluble cellulose-based polymers and polyacrylic acid while the nonadhesive layer is comprised mostly of materials with no adhesive properties. The Suzuki patent does not teach the use of film-forming gels comprised of pH-sensitive polymers and water-insoluble mucoadhesive polymers that form films due to changes in pH and/or desolvation of the polymers. Further, the Suzuki patent does not teach the use of pH-sensitive wax-film composites intended to remain adhered to the skin or mucosal surface for a prolonged period of time.

The Specification at page 2. As the above summary makes clear, Suzuki at least does not teach or suggest a "a pH-sensitive mucoadhesive layer", a limitation of claim 33 and therefore also a limitation of all the other rejected claims, as these all depend from claim 33. *KSR* demands that "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006); see also *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (explaining that an examiner must make "a searching comparison of the claimed invention - including all its limitations - with the teaching of the prior art.") (emphasis added); *CFMT, Inc. v. Yeldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) ("obviousness requires a suggestion of all limitations in a claim") (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). As the Action has not shown how Suzuki teaches or suggests "a pH-sensitive mucoadhesive layer", the Action has not raised a *prima facie* case of obviousness. Applicants therefore respectfully request that this rejection be withdrawn.

Second, while maintaining that claim 33 prior to amendment was not obvious over Suzuki, Applicants have amended claim 33, further making the obviousness rejection moot. As amended claim 33 includes several additional limitations, including (a)(2), that the pH-sensitive

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mucoadhesive layer comprises at least one water-insoluble swellable mucoadhesive polymer, and (c), that the bi-layer wax-film composite comprises at least one molecule of interest. The Action has already conceded that Suzuki does not use the “specific film formers as required in dependent claims 35 and 41.” The Action at page 7.

Regarding limitation (c), Suzuki in fact teaches away from bi-layer wax-film composite comprising at least one molecule of interest. Instead Suzuki teaches a “covering material *consisting essentially* of a cellulose lower alkyl ether and a polyacrylic acid or its pharmaceutically acceptable salt.” Abstract of Suzuki, emphasis added. Applicants note that in patent practice, the transitional phrase “consisting essentially of” is typically interpreted to be limiting to those materials or steps that do not materially affect the basic and novel characteristics of the claimed invention. *See* MPEP § 2111.03. In the case of Suzuki, one such characteristic is using a “medicament-free” covering material. The Abstract of Suzuki teaches that “[a]ccording to the present invention, *without using a medicament*, the injured part on an oral mucosa can be cured rather simply by covering the injured part” (emphasis added). *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994) (“A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.”). Consistent with the Abstract, all the issued claims of Suzuki are directed to a “medicament-free” covering material. Claim 1 of Suzuki reads (emphasis added):

1. A method for treating an injured part on the oral mucosa, which comprises covering the injured part with a covering material consisting of a *medicament-free* adhesive layer consisting essentially of cellulose lower alkyl ether and polyacrylic acid or its pharmaceutically acceptable salt and a *medicament-free* nonadhesive layer which has no adhesion to the wet surface of the oral mucosa.

The two other issued claims in Suzuki depend from claim 1. *See* MPEP § 2141.02[VI] (“A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would

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lead away from the claimed invention.”) (underline in original). Thus, while the Action appears to imply that Suzuki is merely “silent on the use of a pharmaceutical compound” (see the Action at page 6), in fact, Suzuki actively teaches away from using a pharmaceutical compound. In contrast to Suzuki, all the currently pending claims of the present invention require that the bi-layer wax-film composite comprises at least one molecule of interest.

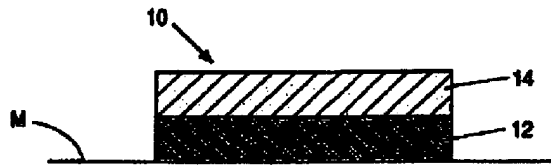
For at least the reasons provided above, the obviousness rejection of claim 33 and all the claims that depend therefrom is both overcome and moot. Applicants therefore respectfully request that this rejection be withdrawn.

## **2. Obvious Rejection over Suzuki in View of Biegajski**

The Action rejects claims 33-47 and 56-57 as obvious over Suzuki in view of U.S. Patent to Biegajski *et al.* (“Biegajski”), alleging that “the substitution of one known element such as the mucoadhesive layer disclosed within Biegajski for another known element such as the mucoadhesive layer disclosed within Suzuki would have yielded predictable results.” The Action at page 7. Applicants have discussed the deficiencies of Suzuki above and have previously noted the deficiencies of Biegajski in an Appeal Brief filed in connection with this Application on June 20, 2005. For at least those reasons, as well as the reasons provided below, and in view of the amendments to claim 33, Applicants submit that the combination of Suzuki and Biegajski does not cure the deficiencies of either reference, nor does it render any of the pending claims obvious.

Biegajski is directed to water soluble pressure-sensitive adhesives that include a water-soluble polymer that is made tacky at room temperature by addition of a water-soluble plasticizer that is miscible with the polymer. Biegajski, Abstract. Figure 1 of Biegajski illustrates a representative bilaminate:

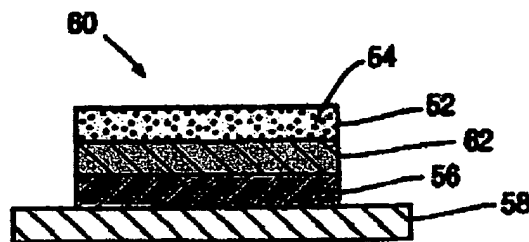
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Here, the basal adhesive layer 12 adheres to mucosal surface M, and upper polymer layer 14 (yellow) and/or basal adhesive layer 12 may deliver substances. Biegajski, column 16, lines 1-24. Upper polymer layer 14 dissolves first and its dissolution is substantially complete when dissolution of the basal adhesive layer 12 begins. *Id.* Biegajski repeatedly explains that each layer is water soluble so that the device can eventually fully dissolve within a body cavity in which it is placed. *See, e.g.,* Biegajski, column 3, lines 35-41, column 4, lines 57-63; column 5, lines 11-15; and column 9, lines 18-22.

In some “trilaminar” embodiments of Biegajski, a third water soluble layer called an occluding layer is placed between, *e.g.,* the two layers shown above. Biegajski explains that this may be useful in situations in which one wants to limit a particular substance in an upper layer from bleeding into the lower layer before the upper layer is completely dissolved—this can be accomplished if the occluding layer is substantially impermeable to the particular substance found in the uppermost layer. *See* Biegajski, column 4, lines 21-46; *see also* column 5, lines 41-54. One disclosed occluding layer is a water-soluble polymer composition with a wax “additive.” Biegajski, column 4, lines 35-39. Another disclosed occluding layer includes a Eudragit family of polymethacrylic copolymers. Biegajski, column 22, lines 4-22. Figure 9 of Biegajski illustrates a representative trilaminar:

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This figure shows polymer layer 52, which contains an active substance, adhesive layer 56, and the additional polymer layer 62 for occlusion (structure 58 is simply a release liner). See Biegajski, column 22, lines 23-32; column 4, lines 35-39 (calling the third layer an occluding layer). The use of the third layer (62), as well as other layers throughout Biegajski allows one to effectively control release rates. See Biegajski, column 4, lines 8-20, 35-46; and column 9, lines 29-32.

The subject matter of claim 33 is clearly and substantially different than the subject matter of Biegajski. First, Biegajski does not disclose, teach or suggest the pH-sensitive mucoadhesive layer comprising at least one pH-sensitive film-forming polymer of claim 33 as currently amended. Particularly, the adhesive layers (e.g., layer 56, above) of Biegajski are not disclosed or suggested as constituting a substance that is affected by changes in pH so that the substance changes conformation, charge, solubility, or combinations thereof. Even if occluding layer 62 of Biegajski includes a Eudragit, there is still no "pH-sensitive mucoadhesive layer" because Biegajski's adhesive layer 56 is not *itself* pH-sensitive—rather, the distinct layer above it may be. Claim 33 recites that it is the mucoadhesive layer that is pH-sensitive, not a separate layer somewhere else in a structure.

Second, Biegajski does not disclose, teach, or suggest the "water-insoluble wax layer" of claim 33. Instead, as mentioned above, Biegajski stresses that for most embodiments the layers should be *water-soluble* so that delivery devices may dissolve completely. See, e.g., Biegajski,

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column 3, lines 35-41, column 4, lines 57-63; column 5, lines 11-15; and column 9, lines 18-22. Biegajski's disclosure of a wax "additive" in a third, water-soluble layer acting as an occluding layer (column 4, lines 35-39) does not amount to disclosure or even a suggestion of a non-soluble wax layer at least because a wax additive is not a layer, and a water-*soluble* layer does not suggest a water-*insoluble* layer.

Third, Biegajski does not disclose, teach, or suggest the "wax-film composite" because a pH-sensitive mucoadhesive layer and water-insoluble wax layer are totally absent. The Action alleges that Biegajski discloses a wax-film composite at column 33, lines 55-60. While this part of Biegajski does feature an embodiment disclosing a layer made of a material that is poorly soluble in water, the embodiment is nevertheless not a "wax-film composite" because this part fails to disclose a wax. That is none of the substances disclosed in lines 55-60, namely, poly(dimethyl siloxane), poly(tetrafluoro ethylene), cellulose acetate, and copolymers of neutral methacrylic acid esters with one or both of methacrylic acid and diethylaminoethyl methacrylate, are waxes or were characterized by Biegajski as waxes.

In sum, and as previously noted in the Appeal Brief filed June 20, 2005, Biegajski fails to teach or suggest any of the following limitation of claim 33:

- (a)(2) pH-sensitive mucoadhesive layer comprising at least one pH-sensitive film-forming polymer,
- (b) water-insoluble wax layer, and
- (preamble) bi-layer wax-film composite.

Combining Suzuki with Biegajski does not cure these deficiencies because the combined teaching still lacks at least a teaching or suggestion for claim 33's (a)(1) element, a pH-sensitive mucoadhesive layer comprising at least one pH-sensitive film-forming polymer. "All words in a



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claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants further note that both references when viewed as a whole teach away from claim 33 and the claims that depend therefrom. A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. MPEP § 2141.02 citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). For example, there is no discernible reason for a skilled artisan to begin with a covering material of Suzuki only to drop the very feature ("medicament-free") that gave it its advantageous properties. See *Eisai Co. Ltd. v. Dr. Reddy's and Teva Pharmaceuticals*, 533 F.3d 1353, 1358 (Fed. Cir., 2008). Similarly, there is no discernible reason for a skilled artisan to begin with a device of Biegajski only to drop the very feature ("water-soluble") that gave it its advantageous properties.

For at least the reasons provided above, the obviousness rejection of claim 33 and all the claims that depend therefrom is both overcome and moot. Applicants therefore respectfully request that this rejection be withdrawn.

### **3. Obvious Rejection over Rajaiah in View of Suzuki and Biegajski**

The Action rejects claims 33-47, 51 and 56-57 as obvious over U.S. Patent 6,677,391 to Rajaiah *et al.* ("Rajaiah") in view of Suzuki and Biegajski. Having discussed the deficiencies of Suzuki and Biegajski above, and in view of the amendments to claim 33, Applicants submit that the combination of Rajaiah, Suzuki and Biegajski does not does not render any of the pending claims obvious. Briefly, Rajaiah teaches creams (Example 1, starting at column 10, line 54) and powders (Example 2, starting at column 11, line 35). Rajaiah also contemplates wafers, non-

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aqueous liquids, aerosols and pastes (column 10, lines 19-28). However, Rajaiah does not disclose or suggest any of the following limitations of claim 33:

- (a)(2) pH-sensitive mucoadhesive layer comprising at least one pH-sensitive film-forming polymer,
- (b) water-insoluble wax layer, and
- (preamble) bi-layer wax-film composite.

As such Rajaiah does not cure the deficiencies resulting from the premised combination of Suzuki and Biegajski. In fact, the Action concedes that "Rajaiah does not recite the use of the specific film formers as required in dependent claims 35 and 41." The Action at page 8. Applicants note that claim 33 does now include the "at least one pH-sensitive film-forming polymer" limitation. As such, this rejection is both overcome and moot. Applicants therefore respectfully request that it be withdrawn.

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Applicants believe that the present document is a full and complete response to the Office Action mailed on December 23, 2008. The present case is in condition for allowance and such favorable action is requested. The Examiner is invited to contact the undersigned Attorney at (512) 536-3116 with any questions, comments, or suggestions relating to the referenced patent application.

Respectfully submitted,



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